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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/555,349	08/01/2000	THOMAS F. TEDDER	180/95/PCT/U	1602

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EXAMINER	
LI, QIAN JANICE	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 06/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/555,349	TEDDER, THOMAS F.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2004* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32 and 33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32, 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on *18 January 2002* is: a)☒ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment after final rejection filed on May 6, 2004 has been entered. Claims 29-31 have been canceled, and claim 33 is newly submitted. Claims 32 and 33 are pending and under current examination.

Claim 32 has been indicated previously as allowable. However, in view of a prior art publication in the information disclosure submitted by the applicants, the Finality is withdrawn in view of new grounds of rejection, and the prosecution is hereby REOPENED.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32 and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are vague and indefinite because of the claim recitation, "highly conserved antigen". The specification fails to define the term, and does not provide a standard for ascertaining the requisite degree with respect to what antigen is considered as highly conserved, and thus the metes and bounds of the claims are unclear.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 32 and 33 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over *Engel et al* (Immunity 1995;3:39-50), in view of *Sato et al* (J Immunol. 1996 Nov 15;157:4371-8, IDS) and *Nielsen et al* (EMBO J 1983;2:115-9).

Engel et al teach immunizing CD19 transgenic mice that overexpress CD19 with an antigen DNP-KLH (step a, page 43, right column). They teach that hCD19 transgenic mice had an overall increase in serum immunoglobulin levels (figure 6B, having antibody-producing cells with disrupted peripheral tolerance). They go on to teach that overexpression of CD19 appears to render B cells more susceptible to differentiation induction (page 44, 2nd paragraph). The data in table 2 show that the levels of isotype IgG2a and IgG2b antibodies are particularly higher in the hCD19 transgenic mice compared to the wild type controls. *Engel et al* do not teach that the hCD19 transgenic mice could be used for production of autoantibody.

Sato et al supplement the teaching of *Engel et al* by disclosing the correlation of increased expression of CD19 with increased levels of endogenous autoantibodies (e.g. abstract). *Sato et al* teach that CD19 serves as a cell surface response regulator that establishes signaling thresholds critical for B lymphocyte development and activation,

particularly the proliferation of a type of B cells, CD5+ B-1 cells (e.g. right column, page 4371), which are known to be associated with the production of autoantibodies and autoimmune diseases. *Sato et al* teach that CD5+ B cells increased significantly in numbers and proportions in mice overexpressing CD19 (Table I). *Sato et al* go on to teach, "INCREASED EXPRESSION OF CD19 MAY ALTERNATIVELY LEAD TO HEIGHTENED RESPONSIVENESS TO WEAK ANTIGENS (highly conserved antigen, noted by the Examiner), RESULTING IN UP-REGULATION OF INNATE IMMUNEITY THAT COULD INADVERTENTLY LEAD TO AUTOIMMUNE DISEASE", and concluded what they have observed in hCD19 transgenic mice mimics a process found in an autoimmune disease, "THEREFORE, THE OVEREXPRESSION OF CD19 RESULTED IN THE PRODUCTION OF ANTI-SSDNA ANTIBODIES OF THE IGG ISOTYPE MAY HAVE CLINICAL SIGNIFICANCE, SINCE THE CLASS SWITCH OF AUTOREACTIVE IGM ABS FROM IGM TO IGG IS ASSOCIATED WITH THE DEVELOPMENT OF LUPUS" (left column, page 4377). Although *Sato et al* do not use an autoantigen to immunize the CD19 transgenic mice, these teachings reasonably suggested to the ordinary skilled in the art that the mice could be used for production of autoantibody. *Engel et al* and *Sato et al* do not teach the process recited in steps (b) to (e) or specific affinity constant of the antibodies.

Nielsen et al supplement *Engel et al* and *Sato et al* by establishing the general method of monoclonal antibody production is well known in the art prior to the instant effective filing date. *Nielsen et al* teach a method of making monoclonal antibody to an antigen (abstract and pages 118-119) comprising obtaining antibody-producing cells (spleen cells) from immunized mice (steps a+b) and fusing them with human melanoma cells (immortalizing cell) to form a hybridoma (steps c+d), which produced antibodies to

an antigen (step e) and obtained antibodies having an affinity constant of greater than $1X10^5$L/mol ($2.5X10^9$L/mol).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings taught by *Engel et al*, *Sato et al* and *Nielsen et al*, by simply using an autoantigen or a weak antigen to immunize a CD19 transgenic mice for production of an autoantiboy as taught by *Engel et al*, and *Sato et al* when such type of antibodies are desired, and proceed with subsequent routine procedures of monoclonal antibody production as taught by *Nielsen et al* with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because it is a practical means for obtaining autoantibodies, which are useful in many diagnostic procedures. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Amy Nelson** can be reached on 571-272-0804. The fax numbers for the organization where this application or proceeding is assigned are **703-872-9306**.

Any inquiry of formal matters can be directed to the patent analyst, **Dianiece Jacobs**, whose telephone number is (571) 272-0532.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist **Rena Jones** whose telephone number is **571-272-0571**.

JANICE LI
PATENT EXAMINER

Q. Janice Li
Patent Examiner
Art Unit 1632

QL
May 28, 2004